

Appl. Serial No. 10/621,803  
Response dated Apr. 29, 2005  
Reply to Office Action of Mar. 16, 2005

REMARKS

Applicant acknowledges receipt of the Communication mailed March 16, 2005.

Group I Claims 1-9 and 19 have been chosen for initial examination on the merits.

Claims 1, 3-7 and 9 are amended herein.

Support for the clarifying amendment of Claim 1 to recite oligonucleotide "primer" can be found in the paragraph bridging pages 13-14 of the Specification.

The amendment of Claim 1 related to a primer "comprising a sequence" clarifies that the immobilized primer can contain target-noncomplementary sequences, such as an upstream promoter sequence. Support for this amendment also can be found in working Example 9.

Support for the amendment of Claim 1 to recite "samples of labeled hybridization probes immobilized in an array" can be found throughout the Specification, including the definition of "array" which appears on page 8, and under the general description of composite arrays which appears on page 13 starting at line 26, and which states:

"Finally, composite arrays include at least one species of hybridization probe which typically is positioned on the surface of the solid support as a pattern of arrayed 'spots' to result in a 'probe array.' The arrayed spots are deposited at discrete locations on the solid support surface such that one spot is spatially separated from another spot in the same array."

Notably, the recitation of "array" in the claims rendered unnecessary the recitation of "at discrete positions," and so those words were deleted from the claims.

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Support for the amendment of Claim 1 concerning each of the recited plurality of samples in the array being "spatially separated from the others, but not spatially separated from said field of immobilized primers" can be found in the Specification on page 14 starting at line 10, where it is stated:

"The immobilized probes and immobilized primers of the composite array also are subject to a preferred distribution pattern. More particularly, the immobilized primers preferably cover the surface of the composite array substantially uniformly except for binding sites on the surface that are occupied by immobilized probe molecules in the array pattern. Unlike the preferred separation of individual spots in the composite array, there is intended to be no spatial separation between the arrayed probes and the immobilized primers. Sites on the solid support surface of the composite array that are not occupied by bonds to the immobilized hybridization probes desirably are occupied by bonds to oligonucleotide primers, thereby resulting in a substantially uniform distribution of primers over the surface of the composite array."

Claim 1 has been amended to specify the presence of a detectable label before the device is contacted with any nucleotide polymerizing enzyme. Support for this amendment can be found in the Specification, for example, on page 6 under the definition of "detectable label"; and in working Example 9 which describes the construction of a device comprising a composite array using chemically synthesized molecular beacon probes labeled with fluorescein. Only after the device was constructed was it contacted with reagents for performing a nucleic acid amplification reaction. Those reagents included a reverse transcriptase (i.e., a DNA polymerizing enzyme) and a T7 RNA polymerase (i.e., an RNA polymerizing enzyme).

Support for the amendment of Claim 1 concerning complementarity between an immobilized probe and an amplicon produced using an immobilized primer can be found, for example, in the Specification on page 11 at lines 10-12; and in working Example 9 (see the full

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paragraph appearing on page 48, and the results appearing in Figures 5C-D). This amendment establishes a relationship between the immobilized probes and primers of the claimed device.

Claims 3-7 and 9 have been conformed with the language of amended Claim 1, and Claims 10-18 and 20-31 have been canceled from the application as being drawn to a nonelected invention.

Claims 1-9 and 19 will be pending after entry of the present Amendment.

Entry of this Amendment is respectfully requested.

**The Rejections Under 35 U.S.C. § 102(b)**

**Keller et al., U.S. Patent No. 5,656,462**

Claims 1-7 and 9 have been rejected under 35 U.S.C. § 102(b) as anticipated by the disclosure contained in U.S. Patent No. 5,656,462 ("Keller"). According to the Office Action, Keller instructs immobilized oligonucleotides and immobilized hybridization probes disposed on the surface of a solid support in accordance with the limitations recited in Claim 1. The reference is further said to disclose other aspects of the invention recited in the rejected dependent claims.

The Keller reference does not anticipate the invention defined by the amended claims because there is no disclosure of primers and labeled probes immobilized to single solid support according to the specified arrangement. Keller teaches a device that includes a solid support, and a single polynucleotide species immobilized to the solid support. More particularly, Keller instructs an immobilized polynucleotide having a 3' oligo(dT) sequence that served as a primer for captured polyA(+) mRNA. There is no teaching or suggestion also to immobilize labeled hybridization probes onto the surface of the solid support; as required by amended Claim 1.

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Rejected Claims 2-7 and 9 all depend from Claim 1, and so incorporate all of the limitations of that amended claim.

Since Keller is deficient in disclosing every element recited in the rejected claims, the reference cannot anticipate Claims 1-7 and 9 under § 102(b). Accordingly, withdrawal of the rejection based on the Keller patent is appropriate.

**Hu et al., WO 01/48242**

Claims 1 and 19 have been rejected under 35 U.S.C. § 102(b) as anticipated by the disclosure contained in the published International Patent Application identified as WO 01/48242 ("Hu"). More particularly, the Examiner has indicated that Hu teaches a device comprising a solid support having a surface, with oligonucleotides immobilized uniformly thereon and hybridization probes immobilized at discrete positions thereon. The rejection further indicates that Hu discloses a kit comprising said device, together with soluble oligonucleotides and a "positive control nucleic acid."

The Hu reference does not anticipate the amended claims because all of the claim limitations are not taught or suggested. Hu instructs a solid support having immobilized thereon a collection of primers in a microarray format (see Abstract). Hu discloses use of the immobilized primers to synthesize nascent strands incorporating a detectable label molecule in a PCR reaction (see page 25 at lines 1-4; and the paragraph bridging pages 25-26), and detection of the amplified and labeled target polynucleotides at each of the original primer locations on the microarray. Hu does not disclose immobilized hybridization probes comprising a detectable label before the device is contacted with a nucleotide polymerizing enzyme, as required by the instant claims. With reference to the rejection of instant Claim 19, Hu describes in paragraph 0090:

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"Where the kit contains a prepared solid support having a set of primers already fixed on the solid support, e.g., for amplifying a particular set of polynucleotides, *the design and construction of such a prepared solid support is described above.*" [all Emphasis added]

Since Hu does not describe a device comprising both immobilized primers and immobilized hybridization probes comprising a detectable label, the disclosed kit cannot be construed as including a device with both of these elements. Moreover, Hu does not even suggest in paragraph 0090 (cited in the Office Action) kits containing a "positive control nucleic acid" that can be amplified by the same primers, but that can be detected by a probe in the composite array that is different from the probe used for detecting analyte amplicon, as described in the instant Specification on page 15 at lines 21-25.

Since Hu fails to disclose every element recited in the rejected claims, the reference cannot anticipate Claims 1 and 19 under § 102(b). Accordingly, withdrawal of the rejection based on the Hu reference is appropriate.

Liu et al., (Anal. Chem. Vol. 71, pp. 5054-5059, 1999)

Claims 1 and 8 have been rejected under 35 U.S.C. § 102(b) as anticipated by the disclosure contained in a scientific journal article by Liu et al., ("Liu"). More particularly, the Examiner has indicated that Liu teaches an optical fiber having immobilized thereto at least one species of oligonucleotide and a plurality of hybridization probes in accordance with Claim 1. The disclosure by Liu of fluorescently labeled molecular beacons as hybridization probes is said in the rejection to anticipate Claim 8.

The Liu reference does not anticipate the amended claims because all of the claim limitations are not taught. Liu describes an optical fiber-based, evanescent wave DNA biosensor consisting of a single species of molecular beacon immobilized to the portion of an optical fiber

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from which a section of outer cladding was removed by chemical etching. The claims have been amended to recite oligonucleotide "primer" which, by the definition appearing in the specification on page 9 at lines 19-24, requires 3'-ends that can be extended by a DNA polymerase activity. Liu describes only molecular beacon hybridization probes having a fluorophore (tetramethylrhodamine), and not a nucleotide substrate, at the 3' terminus. Thus, the molecular beacons of Liu do not qualify as primers having 3'-ends extendable by a DNA polymerase activity. Further, Liu does not describe or suggest immobilizing oligonucleotides other than molecular beacon hybridization probes.

Since Liu does not disclose oligonucleotides corresponding to both the instantly recited primers and hybridization probes, the reference fails to disclose every element recited in the rejected claims, and so cannot anticipate Claims 1 and 8 under § 102(b). Accordingly, withdrawal of the rejection based on the Liu reference is appropriate.

**Conclusion:**

In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of all outstanding objections and rejections are respectfully requested. Allowance of the claims at an early date is solicited. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the telephone number shown below.

Respectfully submitted,

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